

To: Genevieve Matanowski, MD, MPH  
And colleagues on Arsenic Review Panel

From: Arnold Engel, MD, MPH  
And colleagues at CEOH, LLC.

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Re: Need for Rigorous Criteria in Selecting Critical Study for Risk Analysis

The EPA documents do not lay out the criteria for choosing which among many studies should be chosen as the critical study for risk analysis. It is difficult to comment on their choice in the absence of their criteria. Two major studies that have been considered are the SW-Taiwan and NE-Taiwan studies. We present as illustrative examples how a comparison of their data elements and design may facilitate the transparency of study selection.

- 1) Sufficient outcome cases (sum of lung and bladder cancers) to provide a reasonably stable dose response slope

Both the SW and NE-Taiwan by this date have cases counts that are satisfactory for this requirement.

- 2) Sufficient range and relevant distribution of exposure variable (arsenic) to provide a stable dose response slope

Both studies are satisfactory, although the NE study has the advantage of providing more data around 50 ug/liter, which is the dose of special regulatory interest.

- 3) Accuracy of designation of exposure data.

The NE use of individual arsenic determinations is definitely superior to the SW use of the ecological village determination based on median arsenic well water.

- 4) Availability of smoking history.

Smoking history is an important risk factor for both cancers, which is present for the NE and absent for SW.

- 5) Availability of individual data on other cancer risk factors obtained from household interview.

Present for NE and absent for SW.

- 6) Water obtained solely from shallow wells.

True for NE but not SW which has mixture of shallow and artesian wells.

- 7) Contains incident data rather than mortality data.

True for prospective NE but not SW.

- 8) Absence of unique or special characteristics.

False for the Blackfoot Disease (BFD) endemic area of SW; not known for NE.

- 9) Internal consistency in data set with respect to other variables.

Analyses of SW data show internal inconsistency for external variables, such as township and artesian well dependency, and also for internal variables, such single or multiple wells. No such information is known for the NE.

#### Conclusions:

The EPA methodology is lacking in not providing a systematic comparison of potential study choices. As an example of such an approach, the SW and NE-Taiwan studies have been compared for their primary data elements, their secondary and extraneous elements, and their study design. The same can be done with other studies proposed for consideration. This omission of proper study comparisons should be remedied in order that the Panel may adequately assess the EPA's decisions.

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